

### **REMARKS**

Claims 1-5, 7-19, 22, 24, 31, 35, and 48 are pending in the instant application. Claim 48 is withdrawn from consideration for being drawn to a non-elected invention. Claim 35 has been amended to insert the catalog number for the host cell deposited with the NIAID Research and Reference Reagent Program. The amendment includes no new matter.

#### **Withdrawal of Rejections**

Applicant thanks the Examiner for the withdrawal of the rejections of claim 22 for failing to comply with the written description requirement, and withdrawal of the rejection of claims 1, 2, 13, 14, 16, 17, 18, 24, and 31 under 35 U.S.C. §102(b) for being anticipated by Saiga.

#### **Oath/ Declaration**

The Office Action has noted that the Oath and Declaration is defective. A new Oath and Declaration will be provided under a separate cover.

#### **Specification**

A deposit has been made at the NIH AIDS Research & Reference Reagent Program of a cell line of the instant invention. A copy of the data sheet provided by the NIH AIDS Research & Reference Reagent Program providing the Catalog Number is provided herewith.

The paragraphs including blanks have been left in the application in the event that a future deposit is made in relation to the application. Upon indication of allowable matter, paragraphs including blanks will be amended or cancelled.

Claim rejections under 35 U.S.C. §112, first paragraph

Claim 35 has been amended to refer to the deposit made with the NIH AIDS Research & Reference Reagent Program. The NIH AIDS Research & Reference Reagent Program is not a Budapest Treaty recognized repository. However, the cell line is publicly available through the repository.

Claim rejections under 35 U.S.C. §103

*Saiga*

The Office Action has rejected claims 1, 2, 4-9, 13-18, 24, and 31 under 35 U.S.C. §103(a) for allegedly being unpatentable over Saiga et al. (US Patent 6,090,783, hereinafter Saiga). The Office Action states that:

Saiga et al. discloses a gene expression vector comprising a) a promoter, which can be the HIV 5'-LTR, wherein the activity of the promoter is dependent on HIV Tat (see col. 4, lines 4-5; col. 8, lines 57-65; and col. 24, line 63 to col. 25, line 17), b) at least one splice donor site and at least one splice acceptor site (see figure 9 and col. 24, line 63 to col. 25, line 17), c) an expressible non-wild type HIV sequence (e.g., a therapeutic gene, which can be toxic; a reporter gene such as CAT, luciferase, etc.) located between the splice donor and splice acceptor (see col. 4, lines 6-9 and col. 8, line 66 to col. 9, line 17), and d) an RRE from HIV (see col. 9, lines 18-28), wherein the elements are operably linked (see figure 9). The construct can be cloned into an expression vector and transfected into a host cell (see col. 8, lines 47-56).

The Office Action states that although Saiga does not teach the limitation "wherein at least one splice acceptor site is contained within the RRE", it would have been obvious to place the splice acceptor at any location as long as the expressible sequence was between the splice donor and the splice acceptor, and that the splicing of the expressible sequence occurred in the absence of Rev as desired.

The Office Action asserts that absent unexpected results related to the placement of the splice site within the RRE, there is nothing special or unique about placing the splice acceptor site within the RRE rather than downstream from the RRE.

Applicant respectfully disagrees. The reference provides no motivation to alter the position of the acceptor splice site. The *KSR International Co. v. Teleflex Inc.*, (82 USPQ2d 1385 (U.S. 2007)) decision does not abrogate the need for providing some sort of reasoning that one of skill in the art would modify the teachings of a cited reference. Section 2143.01 of the MPEP details situations in which references can and cannot be combined. For example:

IV. Mere statement that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish prima facie obviousness

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art ***is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references.*** *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). \*"[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, ***there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.***" *KSR*, 550 U.S. at \_\_\_, 82 USPQ2d at 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Applicant submits that the assertion that one of skill in the art could move the splice acceptor site is not sufficient motivation to demonstrate that one of skill in the art would move the splice acceptor site.

The Court has addressed the issue of obviousness in chemical cases since the decision of *KSR*. Specifically the Court stated:

While the *KSR* Court rejected a rigid application of the... TSM test in an obviousness inquiry, ***the Court acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination.***

When there is ***a design need or market pressure to solve a problem and there is a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.***" *KSR*, 127 S. Ct. at 1732. \* \* \* That is not the case here. Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad

selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound. *Takeda Chemical Industries Ltd. v. Alphapharm Pty.* 492 F.3d 1350 (Fed. Cir. 2007) [emphasis added]

The Office Action provides no reason that would have prompted one of ordinary skill to combine the elements in the way that the claimed new invention does.

Each the RRE and the splice site present in the constructs of the invention must be functional. The RRE is highly structured to allow for specific binding with Rev (see, e.g., Battiste et al., 1996). Similarly, splice donor and acceptor sites must include specific structural features to allow them to be recognized by the splicing machinery. Those skilled in the art would expect that each RNA structure would best be formed independently of a second RNA structural element, i.e., one of skill in the art would not be motivated to include a splice site within the RRE. As no advantage, and a possible disadvantage, would be expected to be obtained by placing the splice site within the RRE, there can be no motivation to modify Saiga as suggested by the Examiner. Applicant further notes that none of the references cited by the Examiner that teach an RRE and splice sites include a splice site within the RRE, demonstrating that such an arrangement of elements would not be obvious to one of skill in the art.

As claim 1, is not obvious in view of Saiga, and the remaining claims in the rejection contain all of the limitations of claim 1, the remaining claims in the rejection cannot be obvious in view of the cited reference. Withdrawal of the rejection is respectfully requested.

*Corbeau, Hope, D'Costa, and Saiga*

The Office Action has rejected claims 1-18, 24, and 31 under 35 U.S.C. §103(a) for allegedly being unpatentable over Corbeau et al. (U.S. Patent No. 6,323,019, hereinafter Corbeau) in view of Hope et al. (U.S. Patent No. 6,136,597, hereinafter Hope) and D'Costa et al. (Journal of General Virology, 2001, 82:425-434, hereinafter D'Costa) and as evidenced by Saiga et al.

The Office Action states that:

Figure 8B of Corbeau et al. discloses a gene expression vector (pDM128) comprising a) an SV40 promoter, b) at least one splice donor site and at least one splice acceptor site, c) an expressible non-wild type sequence (i.e., CAT gene) located between the splice donor and splice acceptor, and d) an RRE from HIV, wherein the elements are operably linked (see figure 8B). Figure 8B also discloses the 3'-LTR. The construct of Corbeau et al. can be cloned into a vector (see, for example, pDM128) and transfected into host cells (see, for example, col. 17, line 51 to col. 18, line 9).

The Office Action further notes that Corbeau is deficient in at least one of the same teaching as Saiga. Again, the location of the splice acceptor site in Corbeau is downstream of the RRE as shown in Figure 8B. It is not "contained within the RRE" as instantly claimed. For at least the reasons set forth above, it cannot be obvious in view of the cited references to insert the splice acceptor site into the RRE. This deficiency is not overcome by the teachings of either Hope or D'Costa. Applicant submits that the placement of the splice acceptor site downstream of the RRE in both references cited by the Examiner to teach splice acceptor sites demonstrates that it would not be obvious to insert a splice acceptor site in the RRE.

As claim 1, is not obvious in view of Corbeau in combination with Hope, and the remaining claims in the rejection contain all of the limitations of claim 1, the remaining claims in the rejection cannot be obvious in view of the cited references. Withdrawal of the rejection is respectfully requested.

*Saigo or Corbeau in view of D'Costa*

The Office Action has also rejected claim 19 over Saigo or Corbeau in view of D'Costa. As noted in the Office Action and herein, none of the cited references teach or suggest the placement of the splice acceptor site in the RRE. Therefore, the claim cannot be obvious in view of the cited references. Withdrawal is respectfully requested.

The cited references provide no problem to be solved, and no references have been made of record that would motivate one to incorporate the splice acceptor site into the RRE. The MPEP, section 2144 states that

The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, ***that some advantage or expected beneficial result would have been produced by their combination.*** *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). >See also *Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick*, 464 F.3d 1356, 1368, 80 USPQ2d 1641, 1651 (Fed. Cir. 2006)

Having provided no examples of references that teach the incorporation of a splice acceptor site into an RRE, there can be no expected advantage of modifying a reference to include that feature as in the instantly claimed invention. Withdrawal of the rejection is respectfully requested.

*Fee Authorization*

The Commissioner is hereby authorized to charge Deposit Account No. 04-1105 the fees for a three month extension of time for reply, a request for continued examination, and a petition to revive, unintentional abandonment, large entity, referencing Docket No. 59582(47992). It is believed that there is no further fee due with this response. However, if an additional fee is due, with this paper or any other paper filed by this firm in relation to this application, the Commissioner is hereby authorized to charge the Deposit Account indicated above.

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Respectfully submitted,

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